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An alarming public health concern over variability in herbal compositions of marketed immunity booster products during COVID-19: A botanical survey-based study

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Abstract

The world is going through pandemic of the century named COVID-19 disease. The COVID-19 pathogenesis involves cytokine storm in advanced stage leading to systemic hyper-inflammation. Medicinal herbs are practiced as part of alternative therapies in addition to clinically approved drugs with strong belief of its safety and efficacy. In present times, many herbal immunity booster products are available in market which claims to boost immunity for fighting against COVID-19 in prevention and cure. In this study, herbal products with tag of Immunity boosters were surveyed from medical stores and studied for their botanical contents. We surveyed 60 herbal products out of which 31% were tablets and rest were other forms like capsule, decoction and avaleha. Among the products, 17% products were from Dabur followed by Himalaya, Zandu and rest other leading brands of herbal market. Total 98 plants belonging to 50 diverse plant families like Zingiberaceae, Lamiaceae, Piperaceae and Apiaceae were reported being used in these products. Including Fruits (19%), Root (18%) and Leaf (17%), total 20 different plant parts were found used as medicinal herbs. These herbal products were having 10.27 ± 14.02 herbs with range of 56 indicates huge ingredient variation among the products. This diversity in products poses serious health concern in buyers who do not know the safety and efficacy of immunity boosters, being used in COVID-19 pandemic.

Keywords: COVID-19, herbal products, immunity booster, medicinal plants, product survey.

Introduction

For more than a year, COVID-19 has wrecked the world medical health systems and economy at large (Mahapatra and Chandra, 2020). Most countries are struggling to save lives and for treatments or vaccine supply (Fidl, 2020). This severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) associated disease - COVID-19, compelled worldwide researchers to deploy and investigate physio-pathological progression of disease, its spread and treatments (Al-Rohaimi and Al Otaibi, 2020; Meyer, 2020; Rothan and Byrareddy, 2020; Yuen et al., 2020). Three distinct clinical stages of COVID-19 are early infection (stage I), pulmonary phase (stage II) and hyper-inflammation phase (stage III) (Siddiqi and Mehra, 2020). During mild phase, patient

presents a few symptoms like dry cough, fever and malaise with excellent prognosis and recovery if patient can control viral load at this stage. Then infection progresses to viral multiplication, localized inflammation in lungs and pulmonary disease with or without hypoxia in second stage. Possible symptoms are viral pneumonia, cough, fever and possibly hypoxia, with increasing lymphopenia, transaminitis and rising inflammatory markers in blood during this stage. Stage III is marked as extra-pulmonary systemic hyper-inflammation syndrome with elevated levels of pro-inflammatory cytokines such as interleukins (IL-1b, IL-2, IL-6, IL-7, IL-8, IL-17), granulocyte-colony stimulating factor (G-CSF), GM-CSF, macrophase inflammatory protein 1- α (MIP-1α), tumor necrosis factor α (TNF-α), complement 5 (C5) and others (Wu et al., 2020). Markers of multi-organ dysfunction and hyper-coagulability like C-reactive protein, ferritin and D-dimer are also elevated. Decreased CD4 and CD8 T cells, B cells, natural killer cells with elevated neutrophil/lymphocyte ratio reflects the ongoing cytokine storm (Mehta et al., 2020). Secondary hemophagocytic lympho-histiocytosis may happen with elevated Troponin and N-Terminal Pro-B-type Natriuretic Peptide. Such hyperinflammatory stage can be treated with corticosteroids and cytokine inhibitors like tocilizumab (IL-6 antagonist) and anakinra (IL-1 antagonist) or intravenous immune globulin (Qin et al., 2020). During such systemic organ involvement, use of immunomodulatory agents is key to reduce systemic inflammation and rising mortality rate (Qin et al., 2020).

Immunity helps combat infections, which strengthens the concept with large success of vaccination programs in eradicating diseases (Jayawardena et al., 2020; Rappuoli et al., 2014). Major immunity boosters used are diet, fruits, vitamins, antioxidants, probiotics and minerals along with other complementary and alternative medicine approaches like diet, physical exercise, environment and medicinal herbs (Cassa Macedo et al., 2019; Sree Lakshmi and Geetha, 2020). The prime reason behind taking herbal supplements is to improve immunity against systemic infections (Sharma et al., 2019). Herbal supplements and natural-derived compounds are worthy therapeutic alternatives and are explored to combat COVID-19 pathogenesis (Bhattacharya et al., 2021; Boozari and Hosseinzadeh, 2021; Islam et al., 2020). Spices contain many bioactive compounds like Phenols, Flavonoids, alkaloids, tannins, and so on which are known to have positive effect as antiviral and as immunity boosters (Aggarwal et al., 2009; Ogbunugafor et al., 2017). In critical time and panic worldwide, it is reported from India that 71.8% people use Kadha (herbal decoction) and 93.6% people think that spices have beneficial role in COVID-19 prevention (Singh et al., 2021).

In India, according to a report FMCG immunity portfolio unit surged sale by 13.5% in 2020 compared to 3.9% in 2019. Of the sales, turmeric consumption increased to 14.4%, milk food drinks to 6% and chyawanprash by 132% in 2020 (Winkler, 2021). This boost in the market has come with overflowing product list labeled as immunity boosters. In this study, we surveyed such products to understand their herbal composition and their variations with aim to scrutinize effective products. Over the counter these products are sold at large and are being used widely which is concern of public health due to its possible substandard herbal compositions and lack of clinical validations. This article summarizes scientific

analysis of herbal products for their compositions to understand the variability of marketed products.

Materials and Methods

Sample collection

This study was performed during the period of November, 2020 to February, 2021 at Vadodara (22°18'N and 73°12'E), Gujarat, India. The method of sample collection was convenient sampling as per convenient access to the location. Briefly, during the period of work, randomly major medical cum chemist stores were visited for marketed immunity booster products. The chemists were asked for products with tag name of 'immunity boosters', 'general wellness', 'covid-19' and 'health and immunity'. Products with pure herbal ingredients were purchased and included for further analysis. Products with major mineral or other added vitamins were excluded from further analysis to restrict to botanical study.

Content analysis

Purchased herbal products were studied for the manufacturing company, brand name, herbal composition, nutritional value and marketing claim-tag as mentioned in on-pack-information of the product.

Botanical study

The list of plants used in different products were made. The scientific names, vernacular name, part used and family were noted using references. Scientific names of the plants were listed using webpage www.theplantlist.org (visited during February, 2021).

Statistical analysis

Statistical analysis was performed using R programming (RStudio Team, 2021). The graphs and figures were also generated using the same. Frequency, percentage and Mean± standard deviation was used to represent the share of that parameter among other products.

Results

During the survey total 60 products were found matching the inclusion criteria of this study. These products were studied for their details mentioned on package. Of these 60 products, highest form of product found was Tablets (31.6%), followed by Capsules (20%) and Decoction (15%). Other forms of products in market includes Avaleha, Syrup, Juice, Churna, Ark and Jelly. The figure 1 summarizes the forms of products and their fractional share in products studied.

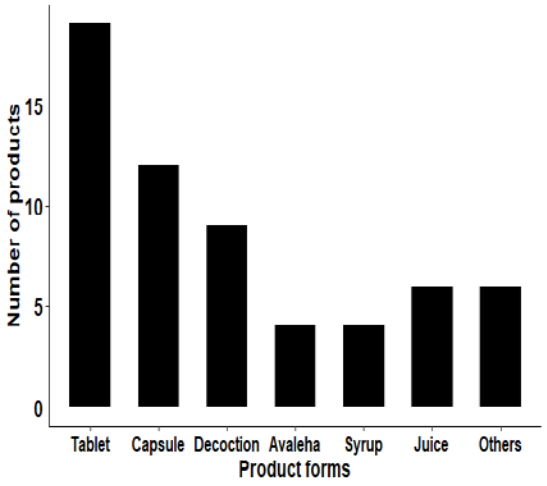

Figure 1. Various forms of products and their frequency is represented with bars.

Further, the analysis of major manufacturing brands revealed total 25 major manufacturing groups in herbal immunity market. In the immunity booster market, major brands observed were Dabur sharing 17% products surveyed, followed by Himalaya (13%), Zandu (13%), Divya (10%), Patanjali (7%) and Apollo life (5%) as shown in figure 2.

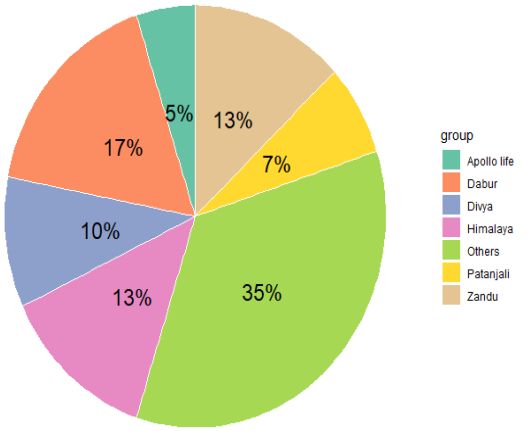

Figure 2. Pie chart showing the share of herbal products by each manufacturing brands. Percentages indicate their relative numbers of products as immunity boosters.

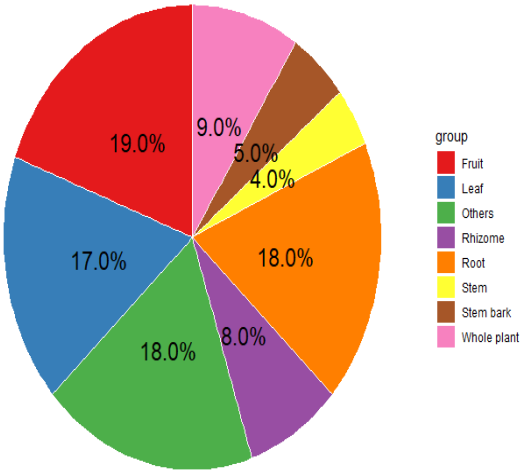

Figure 3. Pie chart showing percentage share of plant part used in herbal products. Percentages in each slice represent their respective weightage.

The figure 2 also highlights the fact that 35% products were of brands other than stated above. It is evident from the data that more than half products are from only a few leading brands. During botanical study, as per Table 1 here, all plants were listed according to information read on the pack of products. In this study, total 98 medicinal herbs were found used in diverse products. Of these, major plant part used were fruit (19%), root (18%) and leaf (17%) followed by rhizome (8%), whole plant (9%), stem bark (5%), stem (4%) and others (18%). The data indicates that more than half plant parts used were fruit, root and leaves of various medicinal plants (Figure 3).

During the survey major plant families were also studied as shown in Figure 4. It is evident that various plant families like Zingiberaceae, Lamiaceae, Piperaceae, Apiaceae, Solanaceae, Fabaceae, Asteraceae, Verbenaceae, Poaceae, Mimosaceae, Convolvulaceae and Combretaceae represent 50% of the plants used in products. However, the richness in diversity of plants utilized as immunity boosters is certain from data of diverse plant families. The medicinal plants reported here are 98 plant species belonging to 80 Genus of 50 diverse plant families with total 20 plant parts used.

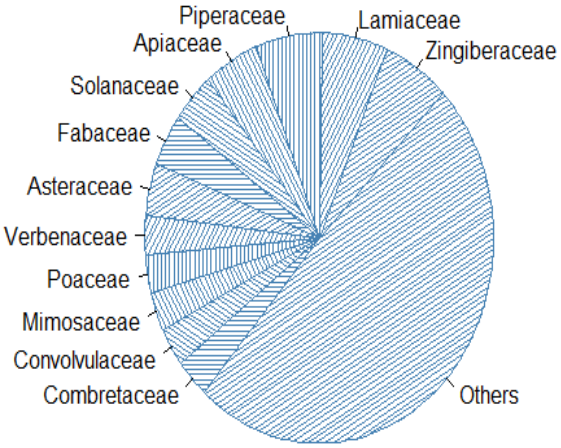

Figure 4. Pie chart showing percentage share of plant families among medicinal plants reported from marketed products. Only major plant families are included in the figure.

98 plant species so reported are medicinally important plants and are used in variety of ethnobotanical formulations and many are used as spices also.

Table 1. List of medicinal plants found in herbal products with their complete botanical details.

Sr. No.	Scientific name	Common name/API name	Part used	Family
1	*Acacia nilotica* (L.) Delile	Gum acacia	Gum	Mimosaceae
2	*Aconitum heterophyllum* Wall. ex Royle	Ativishaa	Rt.	Ranunculaceae
3	*Acorus calamus* L.	Vacha	Rz.	Araceae
4	*Justicia adhatoda* L.	Ardusi	Rt.	Acanthaceae
5	*Albizia lebbeck* (L.) Benth.	Shirish	St.bk.	Mimosaceae
6	*Alpinia galanga* (L.) Willd.	Kulinjana	Rz.	Zingiberaceae
7	*Anacyclus pyrethrum* DC.	Akarkara	Rt.	Asteraceae
8	*Arthrospira platensis* Gomont	Spirullina	Wh.pl.	Microcoleaceae
9	*Asparagus racemosus* Willd.	Shatavari	Rt.	Liliaceae
10	*Azadirachta indica A. Juss.*	Neem	Rt.bk.	Meliaceae
11	*Bacopa monnieri* (L.) Penn.	Brahmi	Wh.pl.	Scrophulariaceae
12	*Bambusa bambos* (L.) Voss.	Vanshlochan	Secretion	Poaceae
13	*Berberis aristata* DC.	Daruharidra	St.	Berberidaceae
14	*Boerhavia diffusa* L.	Punarnava	Wh.pl.	Nyctaginaceae
15	*Boerhavia plumbaginea* Cav.	Shvetpunarnava	Rt.	Nyctaginaceae
16	*Senna alexandrina* Mill.	Maarkandi	Lf.	Caesalpiniaceae
17	*Cassia fistula* L.	Aaragvadha	Fr.P.	Caesalpiniaceae
18	*Cedrus deodara* (Roxb. ex D.Don) G. Don	Devdaru	Ht.wd.	Pinaceae
19	*Centella asiatica* (L.) Urb	Jal brahmi	Wh.pl.	Apiaceae
20	*Chrysopogon zizanioides* (L.) Roberty	Vetiver	Rt.	Poaceae
21	*Cinamomum tamala*(Buch. Ham.) Nees & Eberm	Tamalpatra	Lf.	Lauraceae
22	*Cinamomum zeylanicum* Blume	Dalchini	St.bk.	Lauraceae
23	*Rotheca serrata* (L.) Steane & Mabb.	Bharangi	Rt.	Verbenaceae
24	*Commiphora wightii* (Arn.) Bhandari	Guggul	Resin	Burseraceae
25	*Convolvulus prostratus* Forssk.	Shankhpushpi	Wh.pl.	Convolvulaceae
26	*Coriandrum sativum* L.	Dhana	Fr.	Apiaceae
27	*Cressa cretica* L.	Rudanti	Fr.	Convolvulaceae
28	*Crocus sativus* L.	Kesar	Style	Iridaceae
29	*Cucurbita pepo* L.	Pumpkin	Sd.	Cucurbitaceae
30	*Cuminum cyminum* L.	Swetjiraka	Fr.	Apiaceae
31	*Curcuma longa* L.	Haldi	Rz.	Zingiberaceae
32	*Curcuma zedoaria* (Christm.) Roscoe	White turmeric	Rz.	Zingiberaceae
33	*Cymbopogon citratus* (DC.) Stapf.	Bhutrin	Lf.	Poaceae
34	*Cyperus rotundus*L.	Nagarmotha	Rz.	Cyperaceae
35	*Datura metel* L.	Datura	Lf.	Solanaceae
36	*Desmodium gangeticum* DC.	Sal Leaf bush	Rt.	Fabaceae
37	*Dioscorea bulbifera* L.	Vaaraahi	Tub.rt.	Dioscoreaceae
38	*Eclipta prostrata* Roxb.	Bhringraj	Lf.	Asteraceae
39	*Elettaria cardamomum (Linn.) Maton*	Laghu Ela	Fr.	Zingiberaceae
40	*Embelia ribes Burm. f.*	Vidanga	Fr.	Myrsinaceae

41	*Emblica officinalis* Gaertn.	Amla	Fr.	Euphorbiaceae
42	*Fagonia cretica* L.	Dhanvayaasa	Wh.pl.	Zygophyllaceae
43	*Foeniculum vulgare* Mill.	Variyali	Fr.	Apiaceae
44	*Glycyrrhiza glabra* L.	Mulethi	Rt.	Fabaceae
45	*Gmelina arborea* Roxb.	Cashmere tree	Rt.	Verbenaceae
46	*Hedychium spicatum* Ham. ex Smith.	Shati	Rz.	Zingiberaceae
47	*Inula racemosa* Hook. f.	Pushkaramuula	Rt.	Asteraceae
48	*Mentha piperata* Linn. emend. Huds.	Pudina	Lf.	Lamiaceae
49	*Mesua ferrea* L.	Nagkesar	Stmn.	Guttifereae
50	*Moringa oleifera* Lam.	Drumstick	Lf.	Moringaceae
51	*Moringa peregrina* (Forssk.) Fiori	Shingu	Lf.	Moringaceae
52	*Mucuna pruriens* (L.) DC.	Kaunchbeej	Sd.	Fabaceae
53	*Myristica fragrans* Houtt.	Jaiphal	Sd.	Myristicaceae
54	*Ocimum basilicum* L.	Bhava tulsi	Lf.	Lamiaceae
55	*Ocimum americanum* L.	Kala tulsi	Lf.	Lamiaceae
56	*Ocimum citriodorum* L.	Basil sweet-lemon	Lf.	Lamiaceae
57	*Ocimum gratissimum* L.	Rama tulsi	Lf.	Lamiaceae
58	*Ocimum tenuiflorum* L.	Tulsi	Wh.pl.	Lamiaceae
59	*Operculina turpethum* (L.) Silva Manso	Trivrta	Rt.	Convolvulaceae
60	*Opuntia ficus indica* (L.) Mill.	prickly pear	Fr.	cactaceae
61	*Oroxylum indicum* (L.) Kurz	Shyonak	Fr.	Bignoniaceae
62	*Paederia foetida* L.	Talanili	Wh.pl.	Rubiaceae
63	*Picrorhiza kurroa* Royle ex. Benth.	Katukaa	Rz.	Scrophulariaceae
64	*Piper betle* L.	Nagarvel	Lf.	Piperaceae
65	*Piper cubeba* L. f.	Kankola	Fr.	Piperaceae
66	*Piper longum* L.	Badi pippali	Fr.	Piperaceae
67	*Piper longum* L.	Chhotipipali	St.	Piperaceae
68	*Piper nigrum* L.	Marich	Fr.	Piperaceae
69	*Piper refrofractum* Vahl.	Gajapippali	St.	Piperaceae
70	*Pistacia chinensis* subsp. *Integerrima* (J. L. Stewart ex Brandis) Rech. f.	Kakdasingi	Gl.	Anacardiaceae
71	*Pluchea lanceolata* Oliver & Hiem.	Raasna	Lf.	Asteraceae
72	*Plumbago zeylanica* L.	Chitrak	Rt.	Plumbaginaceae
73	*Prosopis glandulosa* Torr.	Shanta	Lf.	Mimosaceae
74	*Pueraria tuberosa* DC.	Vidarikand	Tub.rt.	Fabaceae
75	*Rhaphanus sativus* L.	Radish	Rt.	Brassicaceae
76	*Rubia cordifolia* L.	Manjishta	Rt.	Rubiaceae
77	*Scindapus officinalis* Schoot.	Gajakrishna	Fr.	Araceae
78	*Sida cordifolia* L.	Bala	Rt.	Malvaceae
79	*Solanum indicum* L.	Kateri	Rt.	Solanaceae
80	*Solanum surattense* Burm. f.	Kantakari	Wh.pl.	Solanaceae
81	*Symplocos racemosa* Roxb.	Lodhra	St.bk.	Symplocaceae
82	*Syzygium aromaticum* (L.) Merr. & M. Perry	Lavang	Fl.bud	Myrtaceae

83	*Syzygium cumini* (L.) Skeels	jamun	Sd.	Myrtaceae
84	*Taxus wallichiana* Zucc.	Talispatra	Lf.	Taxaceae
85	*Terminalia arjuna* W. & A.	Arjuna	St.bk.	Combretaceae
86	*Terminalia bellirica* Roxb.	Bibhitaka	Fr.	Combretaceae
87	*Terminalia chebula* Retz.	Haritaki	Fr.	Combretaceae
88	*Tinospora cordifolia* (Willd.) Miers. ex Hook. f. &Thoms.	Guduchi	St.	Menispermaceae
89	*Trachyspermum ammi* (L.) Sprague	Yavani	Fr.	Apiaceae
90	*Tribulus terrestris* L.	Gokshura	Fr.	Zygophyllaceae
91	*Trichosanthes dioica* Roxb.	Patola	Lf.	Cucurbitaceae
92	*Viola odorata* L.	Banaphsa	Fl.	Violaceae
93	*Vitex negundo* L.	Negundi	Fr.	Verbenaceae
94	*Vitis vinifera* L.	Draksha	Fr.	Vitaceae
95	*Withania somnifera* (L.) Dunal	Ashwagandha	Rt.	Solanaceae
96	*Woodfordia fruticosa* (L.) Kurz.	Dhaataki	Fl.	Lythraceae
97	*Zanthoxylum armatum* DC.	Tejohva	St.bk.	Rutaceae
98	*Zingiber officinale* Roscoe	Sounth	Rz.	Zingiberaceae
Rt.=Root; Rz.=Rhizome; St.=Stem; St.bk.=Stem bark; Fl.=Flower; Lf.=Leaf; Fr.=Fruit; Rt.bk.=Root Bark; Sd.=Seed; Fl.bud=Floral bud; Wh.pl.=Whole plant; Tub.rt.=Root tuber; Gl.=Gall; Stmn.=Stamen; Fr.p.=Fruit pulp; Ht.wd.=Heart wood				

It was found that range of plants added in each produce was as low as 1 ingredient to as high as 56 ingredients per product. The mean ingredients per product was 10.27 herbs with standard deviation of ±14.02. The data indicates very high variability in numbers of ingredients used per product.

Discussions

COVID-19 pathogenesis involves the cytokine storm which leads to multi-organ failure (Mehta et al., 2020), this is where traditional herbal system can aid in reducing effects of pro-inflammatory cytokines. Numbers of Indian herbs are known to have immuno-modulatory effects with their therapeutic potential to target inflammatory diseases (Ren et al., 2017). Such herbal immuno-modulators like *Withania somnifera* and *Tinospora cordifolia* can stimulate or suppress the components of innate and adaptive, both immune systems (Singh et al., 2016). Many Chinese traditional medicines have also been reported to have effective improvement in chronic inflammation and modulation of cytokine levels in lungs, esophagus, cerebrum, colon, skin, prostate, mammary gland, liver and pancreas (Ichikawa et al., 2003; Khatami, 2009). A few plants reported here like *Zingiber officinale*, *Curcuma longa*, *Glycyrrhiza glabra, Rubia cordifolia* and *Zanthoxylum armatum* have been reported in blood and lymph diseases, autoimmune diseases, atherosclerosis and pain (Pan et al., 2011). These herbal medicines during COVID-19 pandemic have become more popular due to limitations of clinical intervention. Commonly used alternative approach includes dietary supplements and botanicals available in market with more belief of lesser side effects (Rathore et al., 2007). It is also reported that outcomes of natural extracts is inconsistent mostly due to method of extract, and is key factor to consider for reason that each herb is mixture of plenty pharmacological active

compounds (Ghasemian et al., 2016).

In current study, data of 60 marketed products with tag name of Immunity boosters is presented. In India, the herbal product manufacturer were largely either unaware of guidelines of good agricultural and collection practices imposed by National Medicinal Plant Board or they find it impractical, due to which quality of products are unregulated (Sahoo and Manchikanti, 2013). This report has mentioned 150 herbal product manufacturers across country, and our data has reported 25 manufacturers which counts to be 17%. This under reporting percentage may be due to our exclusion criteria of products, time period of the study as well as sample collection method. Further, here we reported total 11 forms of products of which 6 major types Tablets, Capsule, Decoction, Avaleha, Juice and syrup are predominant forms in Indian market. For decoction, each herbal component of AYUSH kwath is already reported to have some role in immunomodulation and such poly-herbal formulations are known to have more efficacy with minimal side effect (Gautam et al., 2020; Karole et al., 2019). This study reports 68.3% products as polyherbal formulations with more than two herbs, due to which it may have minimal side effects.

The medicinal plants reported in this study are of diverse kinds, as evident from diversity of plant families. Further, the variability of plants used as immunity booster is major concern of public health as these products are sold over the counter. The variations in herbal source, labeling, packaging and preparation are major concern for public health as more than 40% poly-herbal formulations fail to contain ingredients as claimed on pack (Tachjian et al., 2010). It was reported in high-pressure liquid chromatographic analysis, to contain a controlled steroid, testosterone in over-the-counter available dietary supplements (Green et al., 2001). The buyer's behavior is also influenced by variety of social media which largely involves commercial interest and is merely a scientific rhetoric (Wagner et al., 2020). Such studies are out of the scope of this article but we propose that more scientific validation of these herbal products should be performed for confirming the purity and efficacy of herbal products. We hence propose considering public health concern, the immunity booster label should be used more appropriately on clinically validated products only.

Conflict of interest

Authors declare that there is no conflict of interest.

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